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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/928,434	08/14/2001	Makoto Inada	04676.0071	8134

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EXAMINER

HARTLEY, MICHAEL G

ART UNIT

PAPER NUMBER

1616

DATE MAILED: 07/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/928,434

Applicant(s)

INADA ET AL.

Examiner

Michael G. Hartley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 May 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 6-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Response to Amendment

The amendment filed 5/29/2003 has been entered. Claim 5 has been canceled. Claims 1, 3, 4 and 6-15 have been amended. New claims 16-19 have been added.

Response to Arguments

Applicant's arguments with respect to claims 1-4 and 6-19 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by el Kouni (5,670,331).

El Kouni discloses compositions comprising 5-fluorouracil, see abstract. Since C-13, N-15 and O-18 all have a natural abundance, the 5-fluorouracil compositions would inherently be labeled therewith. Also, it is noted that since claim 1 fails to recite any specific label, only that it is non-radioactive. Since any atom may be a label (i.e., depending on the method of detection), 5-fluorouracil, which contains hydrogen atoms, would be within the scope of claim 1, (e.g., hydrogen may be label for methods of NMR). Since the compound is the same, it must inherently have the same functional properties (i.e., acting as a substrate for an enzyme) as set forth in claims 2-3. Same compounds must have the properties. Also, the intended use of the claimed invention has not been given patentable weight herein, as intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). The 5-fluorouracil is an oral medication, thus would be expected to be in an oral form. However, it is noted that for oral administration is an intended use recitation.

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Claims 1-4 and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Fujii (US 4,328,229).

Fujii discloses an oral composition comprising 5-FU or uracil and acceptable carriers, see abstract and column 2. As stated above, since C-13, N-15 and O-18 are naturally abundant, these compounds would inherently be labeled with such isotopes. Also, since claims 1-3 fail to recite a label, the hydrogen on the compounds would be within the scope of a non-radioactive label, as it can be detected using NMR.

Claims 1-4 and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Triplett (PTO-892, J. of Labeled Compound and Radiopharm., 1978).

Triplett discloses carbon-13 labeled uracil, see abstract. As stated above, the intended use must result in a structural difference and none is seen between the C-13 labeled uracil of Triplett and that claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4 and 6-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over either one of el Kouni (5,670,331) or Creasey (PTO-1449, Clinical Pharm. And Therap.) in view of Katzman (US 5,944,670).

El Kouni discloses compositions comprising 5-fluorouracil and methods of determining pyrimidine metabolism comprising administering radiolabeled forms thereof, see examples 5 and 9. The methods of

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el Kouni include determining the safe dose of the drug and comparison with health subjects, see columns 4 and 10.

Creasey discloses a method of determining pyrimidine metabolism comprising administering a C-14 labeled 5-fluorouracil for determination of dosage, see abstract and page 274.

El Kouni and Creasey fail to specifically disclose a method using C-13, N-15 or O-18 as a label.

However, it is known in the art that such non-radioactive labels may be used in an equivalent manner to the radiolabels disclosed by el Kouni and Creasey, as shown by Katzman.

Katzman teaches that various labels, such as, C-13 and C-14 may be used interchangeable and may be used for breath tests which administer labeled compounds and teaches that C-13 is preferred because it avoids the use of radioactivity, see column 4, lines 20+. Katzman also teaches that metabolism of such labeled compounds may be easily detected using breath tests, see abstract.

It would have been obvious to one of ordinary skill in the art to modify the compositions and methods disclosed by el Kouni or Creasey to substitute C-13 for C-14 because it is known in the art that such labels are equivalents and may be used interchangeably, as shown by Katzman. One of ordinary skill in the art would have been motivated to employ a non-radioactive label in the compositions and methods disclosed by el Kouni or Creasey to gain the advantage of not having to deal with the precautions associated with radioactivity, as taught by Katzman.

Further, it would have been obvious to one of ordinary skill in the art to further modify the methods disclosed by el Kouni or Creasey to employ a breath test because breath tests are well known to be an safe and effective means to measure the metabolism of such labeled compounds, as taught by Katzman.

Claims 1-4 and 6-8 and 10-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abramson (6,355,416).

Abramson discloses compositions comprising non-radioactively labeled compounds. The compounds include thymine, see claim 5. The labeled compounds are used in methods of determining pyrimidine metabolism comprising administering radiolabeled forms thereof, note that the uptake of the

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thymine in DNA in the body is within the scope of metabolism, see column 5, lines 14+. The labels include C-13 and N-15, see columns 9-10. Oral administration of such tracers is suggested in example 1.

Abramson fails to specifically disclose a composition (i.e., exemplify) a composition comprising C-13 labeled thymine and methods of determining metabolism thereof.

However, it would have been obvious to one of ordinary skill in the art to have labeled thymine with C-13 for said methods because Abramson clearly teaches that thymine may be used as a tracer by being labeled with C-13 for methods to measure DNA synthesis rates, which would be a metabolic use of thymine.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

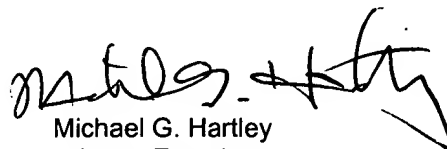
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (703) 308-4411. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the organization where

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this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



Michael G. Hartley
Primary Examiner
Art Unit 1616

MH
July 19, 2003